CENTER FOR DRUG EVALUATION AND RESEARCH

Approval Package for:

Application Number : 064153

Trade Name : STERILE BACITRACIN USP 50,000 UNITS/VIAL

Generic Name: Sterile Bacitracin USP 50,000 units/vial

Sponsor : Pharma-Tek, Inc.

Approval Date: May 9, 1997

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION 064153

CONTENTS

	Included	Pending Completion	Not Prepared	Not Required
Approval Letter	X			
Tenative Approval Letter				
Approvable Letter				
Final Printed Labeling	X			
Medical Review(s)				
Chemistry Review(s)	X			
EA/FONSI				
Pharmacology Review(s)				
Statistical Review(s)				
Microbiology Review(s)				
Clinical Pharmacology Biopharmaceutics Review(s)				
Bioequivalence Review(s)	X			
Administrative Document(s)				
Correspondence				

CENTER FOR DRUG EVALUATION AND RESEARCH

Application Number 064153

APPROVAL LETTER

)A 64-153

MAY – 9 1997

Pharma-Tek, Inc.
Attention: Susan E. Badia
P.O. Box 1920
Huntington, NY 11743

Dear Madam:

This is in reference to your abbreviated antibiotic application dated June 27, 1995, submitted pursuant to Section 507 of the Federal Food, Drug, and Cosmetic Act, for Sterile Bacitracin USP, 50,000 units/vial.

Reference is also made to your amendment dated February 28, and March 21, 1997.

We have completed the review of this abbreviated application and have concluded that the drug is safe and effective for use as recommended in the submitted labeling. Accordingly, the application is approved. The Division of Bioequivalence has determined your Sterile Bacitracin USP, 50,000 units/vial to be bioequivalent and, therefore, therapeutically equivalent to the listed drug, Sterile Bacitracin USP, 50,000 units/vial by Pharmacia and Upjohn Company.

Under 21 CFR 314.70, certain changes in the conditions described in this abbreviated application require an approved supplemental application before the change may be made.

Post-marketing reporting requirements for this abbreviated application are set forth in 21 CFR 314.80-81. The Office of Generic Drugs should be advised of any change in the marketing status of this drug.

We request that you submit, in duplicate, any proposed advertising or promotional copy which you intend to use in your initial advertising or promotional campaigns. Please submit all proposed materials in draft or mock-up form, not final print. Submit both copies together with a copy of the proposed or final printed labeling to the Division of Drug Marketing, Advertising, and Communications (HFD-240). Please do not use Form FD-2253 (Transmittal of Advertisements and Promotional Labeling for Drugs for Human Use) for this initial submission.

We call your attention to 21 CFR 314.81(b)(3) which requires that materials for any subsequent advertising or promotional campaign be submitted to our Division of Drug Marketing, Advertising, and Communications (HFD-240) with a completed Form FD-2253 at the time of their initial use.

Sincerely yours,

/S/

Douglas L. Sporn
Director
Office of Generic Drugs
Center for Drug Evaluation and Research

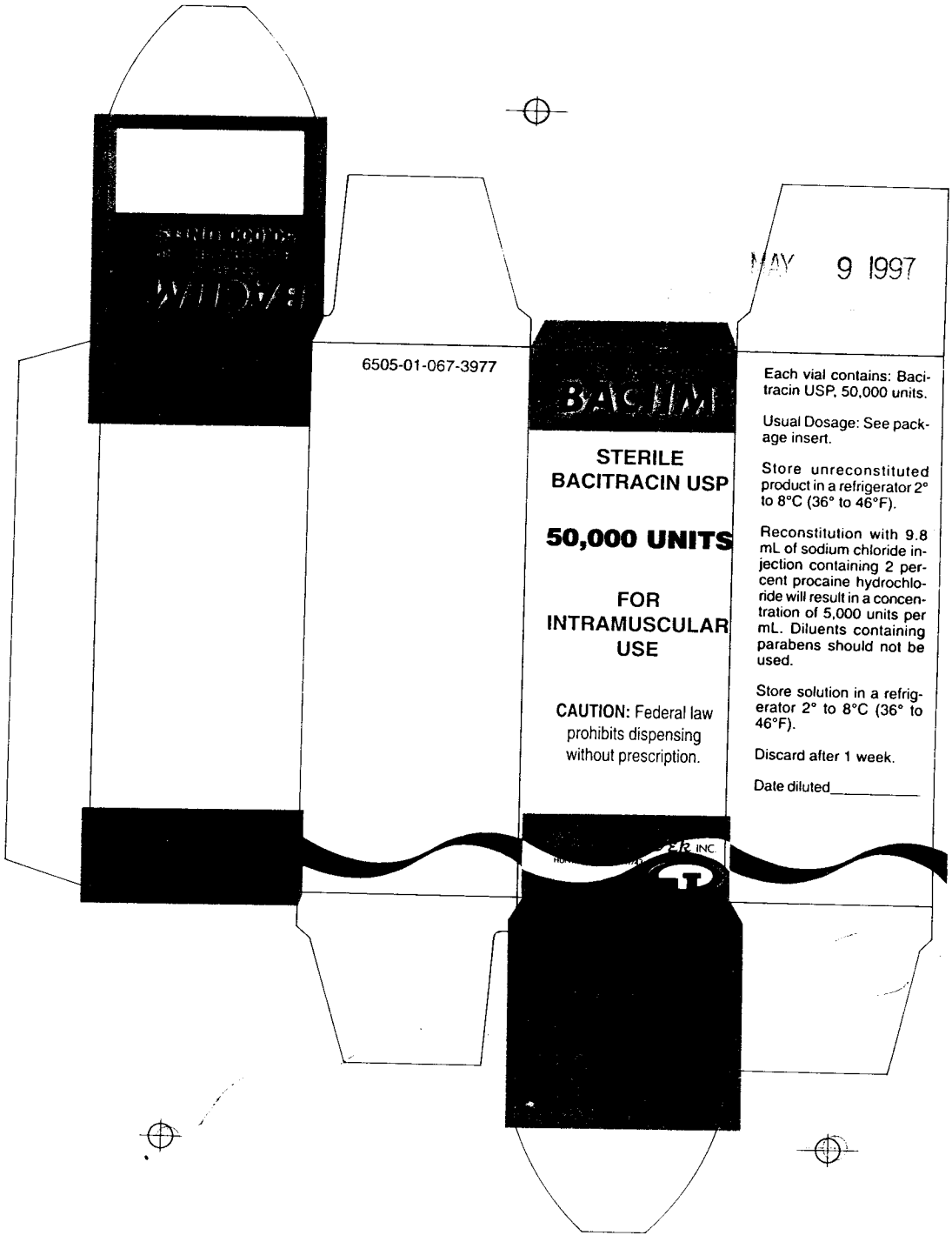
5/8/97

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER 064153

FINAL PRINTED LABELING

CARTON LABELING



[redacted]

STERILE
BACITRACIN USP
50,000 UNITS
FOR
INTRAMUSCULAR USE

CAUTION: Federal law prohibits dispensing without prescription.

6505-01-067-3977
Each vial contains: Bacitracin USP, 50,000 units.
Usual Dosage: See package insert.
Store unreconstituted product in a refrigerator 2° to 8°C (36° to 46°F).

Reconstitution with 9.8 mL of sodium chloride injection containing 2 percent procaine hydrochloride will result in a concentration of 5,000 units per mL. Diluents containing parabens should not be used.

Store solution in a refrigerator 2° to 8°C (36° to 46°F).

Discard after 1 week.

Date diluted_____

Manufactured by:
Ben Venue Laboratories, Inc.
Bedford, OH 44146

Q 1007

MAY 9 1997

Pharma-Tek

BACIIM™

STERILE BACITRACIN USP

WARNING

Nephrotoxicity: Bacitracin in parenteral (intramuscular) therapy may cause renal failure due to tubular and glomerular necrosis. Its use should be restricted to infants with staphylococcal pneumonia and empyema when due to organisms shown to be susceptible to bacitracin. It should be used only where adequate laboratory facilities are available and when constant supervision of the patient is possible.

Renal function should be carefully determined prior to and daily during therapy. The recommended daily dose should not be exceeded and fluid intake and urinary output maintained at proper levels to avoid kidney toxicity. If renal toxicity occurs the drug should be discontinued. The concurrent use of other nephrotoxic drugs, particularly streptomycin, kanamycin, polymyxin B, polymyxin E (colistin), neomycin, and viomycin, should be avoided.

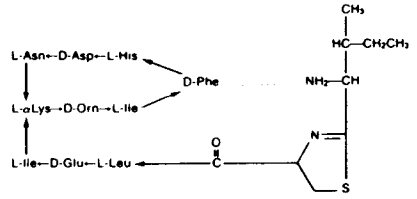
DESCRIPTION

The vial content of Sterile Bacitracin USP is sterile. The therapeutic class of the drug is antibacterial and is intended for intramuscular use. Bacitracin is an antibiotic polypeptide complex and its major component is bacitracin A which has a molecular weight of 1422.7.

Each vial contains 50,000 units of bacitracin.

Bacitracin is a white to pale buff, hygroscopic powder, odorless or having a slight odor. It is freely soluble in water; insoluble in acetone, chloroform, and ether. While soluble in alcohol, methanol, and glacial acetic acid, there is some insoluble residue. It is precipitated from its solutions and inactivated by many of the heavy metals.

The structural formula is:



bacitracin A

The molecular formula is: $C_{66}H_{103}N_{17}O_{16}S$

CLINICAL PHARMACOLOGY

Bacitracin, an antibiotic substance derived from cultures of *Bacillus subtilis* (Tracey), exerts pronounced antibacterial action *in vitro* against a variety of gram-positive and a few gram-negative organisms. However, among systemic diseases, only staphylococcal infections qualify for consideration of bacitracin therapy. Bacitracin is assayed against a standard and its activity is expressed in units, 1 mg having a potency of not less than 50 units.

Susceptibility plate testing: If the Kirby-Bauer method if disk susceptibility is used, a 10 unit bacitracin disk should give a zone of over 13mm when tested against a bacitracin-susceptible strain of *Staphylococcus aureus.* Absorption of bacitracin following intramuscular injection is rapid and complete. A dose of 200 or 300 units/kg every 6 hours gives serum levels of 0.2 to 2 mcg/ml in individuals with normal renal function. The drug is excreted slowly by glomerular filtration. It is widely distributed in all body organs and is demonstrable in ascitic and pleural fluids after intramuscular injection.

INDICATIONS AND USAGE

In accord with the statements in the "Warning Box" the use of intramuscular bacitracin is limited to the treatment of infants with pneumonia and empyema caused by staphylococci shown to be susceptible to the drug.

CONTRAINDICATIONS
This drug is contraindicated in those individuals with a history of previous hypersensitivity or toxic reaction to it.

PRECAUTIONS
See "Warning Box" for precautions in regard to kidney toxicity associated with intramuscular use of bacitracin.

Adequate fluid intake should be maintained orally, or if necessary, by parenteral method.

As with other antibiotics, use of this drug may result in overgrowth of nonsusceptible organisms, including fungi. If superinfection occurs, appropriate therapy should be instituted.

ADVERSE REACTIONS
Nephrotoxic reactions. Albuminuria, cylindruria, azotemia. Rising blood levels without any increase in dosage.

Other reactions. Nausea and vomiting. Pain at site of injection. Skin rashes.

DOSAGE AND ADMINISTRATION
TO BE ADMINISTERED INTRAMUSCULARLY ONLY

Infant dose: For infants under 2500 grams—900 units/kg/24 hours in 2 or 3 divided doses. For infants over 2500 grams—1,000 units/kg/24 hours, in 2 or 3 divided doses. Intramuscular injections of the solution should be given in the upper outer quadrant of the buttocks, alternating right and left and avoiding multiple injections in the same region because of the transient pain following injection.

Preparation of Solutions—Should be dissolved in sodium chloride injection containing 2 percent procaine hydrochloride. The concentration of the antibiotic in the solution should not be less than 5,000 units per ml nor more than 10,000 units per ml.

Diluents containing parabens should not be used to reconstitute bacitracin; cloudy solutions and precipitate formation have occurred.

Reconstitution of the 50,000 unit vial with 9.8 ml of diluent will result in a concentration of 5,000 units per ml.

Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit.

HOW SUPPLIED
Sterile Bacitracin USP is available in vials containing 50,000 units. NDC 39822-0255-5.

Store the unreconstituted product in a refrigerator 2° to 8°C (36° to 46°F). Solutions are stable for one week when stored in a refrigerator 2° to 8°C (36° to 46°F).

Caution: Federal law prohibits dispensing without prescription.

Manufactured by
Ben Venue Laboratories, Inc. • Bedford, OH 44146

Distributed by
Pharma-Tek INC
HUNTINGTON, NY 11743

Printed in U.S.A. Revised Feb. 1997

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER 064153

CHEMISTRY REVIEW(S)

1. CHEMISTRY REVIEW NO. 3

2. AADA # 64-153

3. NAME AND ADDRESS OF APPLICANT

Pharma-Tek, Inc.
Attention: Susan E. Badia
P.O. Box 1920
Huntington, NY 11743

4. BASIS OF SUBMISSION

Sterile Bacitracin USP
The Upjohn Company
21 CFR Section 448.10a

5. SUPPLEMENT(s)

N/A

6. PROPRIETARY NAME
BACI-IM

7. NONPROPRIETARY NAME
Sterile Bacitracin USP

8. SUPPLEMENT(s) PROVIDE(s) FOR:
N/A

9. AMENDMENTS AND OTHER DATES:

Date of Application: June 27, 1995
Date of Receipt: June 28, 1995
Date acceptable for filing: August 21, 1995
Acknowledge Letter Dated: September 20, 1995
Amendment dated August 18, 1995
Amendment dated August 23, 1995
Amendment dated October 15, 1996
Amendment dated February 28, 1997 (Subject of this review)

10. PHARMACOLOGICAL CATEGORY
Antibiotic

11. Rx or OTC
Rx

12. RELATED IND/NDA/DMF(s)

(b)4 - Confidential Business

(b)4 - Confidential Business

13. DOSAGE FORM
Lyophilized Powder for Reconstitution

14. POTENCY
50,000 units per vial

15. CHEMICAL NAME AND STRUCTURE
Bacitracin A

$C_{66}H_{103}N_{17}O_{16}S$

16. RECORDS AND REPORTS
N/A

17. COMMENTS
Applicant's response dated February 28, 1997, to our FAX dated 2/24/97 is as follows:

(b)4 - Confidential Business

Request for waiver denied

18. CONCLUSIONS AND RECOMMENDATIONS

The application may be approved with an acceptable EER for

(b)4 - Confidential Business

19. REVIEWER: Vernon C. Walton

DATE COMPLETED: 3/17/97.

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER 064153

BIOEQUIVALENCE REVIEW(S)

AADA 64-153

JAN 25 1996

Pharma-Tek, Inc.
Attention: Susan E. Badia
P.O. BOX 1920
Huntington NY 11743

Dear Madam:

Reference is made to your abbreviated antibiotic application dated August 18, 1995, submitted pursuant to Section 507 of the Federal Food, Drug and Cosmetic Act for Sterile Bacitracin USP, 50,000 units/vial.

The following comments pertain only to bioequivalency issues in the August 18, 1995 submission.

> The Division of Bioequivalence has completed its review and has no further questions at this time.

Please note that the bioequivalency comments expressed in this letter are preliminary. The above bioequivalency comments may be revised after review of the entire application, upon consideration of the chemistry, manufacturing and controls, microbiology, labeling or other scientific or regulatory issues. A revised determination may require additional information and/or studies, or may conclude that the proposed formulation is not approvable.

Sincerely yours,

[redacted](b)4 -[redacted]
Confidentia

Keith K. Chan, Ph.D.
Director, Division of Bioequivalence
Office of Generic Drugs
Center for Drug Evaluation and Research

V1V

JAN 15 1996

Bacitracin
Lyophilized Cake
Injection; 50,000 Units/Vial
AADA #64-153
Reviewer: L. Chuang

Pharma-Tek Inc.
Huntington, N.Y.
Submission Date:
August 18, 1995

Review of a Waiver Request for an Injectable Dosage Form

Bacitracin is a hygroscopic powder which is freely soluble in water. It is an antibiotic substance derived from cultures of *Bacillus subtilis*, exerts pronounced antibacterial action *in vitro* against a variety of gram-positive and a few gram-negative organisms.

This product is being made available as a lyophilized sterile powder in a vial containing 50,000 units of bacitracin. After reconstitution in 9.8 mL of diluent (sodium chloride injection containing 2 percent procaine hydrochloride), the resulted clear solution is indicated for intramuscular injection in the treatment of infants with pneumonia and empyema caused by staphylococci shown to be susceptible to the drug.

The listed reference product is Bacitracin Injectable, 50,000 unit/vial, by Upjohn Co. approve under NDA #60733 on 07/29/48.

At present, The Upjohn Company is the only active US manufacturer of the product under an approved NDA (NDA #60733). Pharma-Tek currently market this product as a distributor under the Upjohn's NDA. In the present [redacted](b)4 - Confidential[redacted] ing approval of the test product by [redacted] as a contract manufacturer for Pharma-Tek Inc..

The firm requests that the in-vivo bioequivalence requirements for its Bacitracin Injection, 50,000 units/vial, manufactured by [redacted] [redacted](b)4 - Confidential[redacted] e waived. The comparative formulations of the firm's test product versus the reference product (Upjohn) are presented below:

Firm	Pharma-Tek	Upjohn
Dosage Form	Lyophilized Cake	Lyophilized Cake
Ingredient	**Amount per Vial**	
Bacitracin USP	50,000 units	50,000 units
Water for Injection	Removed during lyophilization cycle	--
Nitrogen, NF	Used to provide inert atmosphere	--

Nitrogen, NF	Used to provide inert atmosphere	--

Comments:

1. The test product is a parenteral solution after reconstitution with diluent and intended solely for administration by injection (IM).

2. The test product contains the same active ingredient as Upjohn's Bacitracin for Injection, 50,000 units/vial, approved under NDA #60733. The vials are not labeled to contain any preservatives or other material.

Recommendation:

The Division of Bioequivalence agrees that the information submitted by Pharma-Tek Inc. demonstrates that Bacitracin Injection, 50,000 units/vial, falls under 21 CFR Section 320.22 (b)(1) of the Bioavailability/Bioequivalence Regulations. The waiver of in-vivo bioequivalence study for the firm's Bacitracin Injection, 50,000 units/vial, is granted. From the bioequivalence point of view, the Division of Bioequivalence deems the test injectable formulation to be bioequivalent to Bacitracin Injection, 50,000 units/vial, manufactured by The Upjohn Company.

/S/ 1/15/96

Lin-whei Chuang
Division of Bioequivalence
Review Branch I

RD INITIALED YHUANG
FT INITIALED YHUANG /S/ 1/5/96

cc: AADA 64-153 (original, duplicate), HFD-600 (Hare), HFD-630, HFD-652 (Huang, Chuang), Drug File, Division File.

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